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ATTORNEY DOCKET NO. 10010791-1

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

Inventor(s): Douglas A. Amorese

Serial No.: 09/870,939 Examiner: Betty J. Forman

Filing Date: May 30, 2001 Group Art Unit: 1634

Title: COMPOSITE ARRAYS

COMMISSIONER FOR PATENTS
P.O. Box 1450
Alexandria VA 22313-1450

TRANSMITTAL OF APPEAL BRIEF

Sir:

Transmitted herewith is the Appeal Brief in this application with respect to the Notice of Appeal filed on November 17, 2004 .

The fee for filing this Appeal Brief is (37 CFR 1.17(c)) $500.00

(complete (a) or (b) as applicable)

The proceedings herein are for a patent application and the provisions of 37 CFR 1.136(a) apply.

☐ (a) Applicant petitions for an extension of time under 37 CFR 1.136 (fees: 37 CFR 1.17(a)(1)-(5)) for the total number of months checked below:

☐	one month	$ 110.00
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☐ The extension fee has already been filled in this application.

☒ (b) Applicant believes that no extension of term is required. However, this conditional petition is being made to provide for the possibility that applicant has inadvertently overlooked the need for a petition and fee for extension of time.

Please charge to Deposit Account **50-1078** the sum of $ 500.00. At any time during the pendency of this application, please charge any fees required or credit any overpayment to Deposit Account **50-1078** pursuant to 37 CFR 1.25.

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Date of Facsimile: 01-11-2005 703-872-9306

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Respectfully submitted,

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APPELLANTS' BRIEF Address to: Box DAC Assistant Commissioner for Patents Alexandria, VA 22313-1450	Attorney Docket	10010791-1
	First Named Inventor	Douglas A. Amorese
	Application Number	09/870,939
	Filing Date	May 30, 2001
	Group Art Unit	1634
	Examiner Name	Betty J. Forman
	Title	*COMPOSITE ARRAYS*

Sir:

This Appeal Brief is filed in support of Appellants' appeal of the Examiner's Final Rejection dated August 17, 2004. A Notice of Appeal was filed by fax on November 17, 2004. As such, this Appeal Brief is timely filed.

This Appeal Brief is believed to be compliance with 37 C.F.R § 41.37, as amended by the final rule changes effective on September 13, 2004.

Please charge the $500.00 fee for filing this Brief to our Deposit Account No. 50-1078. If this fee is incorrect, please charge or credit the account accordingly.

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REAL PARTY IN INTEREST

The real party in interest in this appeal is Agilent Technologies.

RELATED APPEALS AND INTERFERENCES

There are no related appeals or interferences.

STATUS OF THE CLAIMS

Claims 1-3, 5-20 and 38-41 are pending and are rejected. Claims 4 and 31-37 are cancelled. Claims 1-3, 5-20 and 38-41 are appealed.

STATUS OF AMENDMENTS

As indicated on page 2 of the Final Office Action dated August 17, 2004 (termed herein the "FOA"), all claim amendments have been entered.

Appendix I sets forth the currently pending claims. All of the pending claims are appealed.

SUMMARY OF THE CLAIMED SUBJECT MATTER

The appealed claims relate to polynucleotide arrays containing: a) a first set of features that contain single stranded cDNA molecules that are at least 400 nucleotides in length and b) a second set of features that are independent of the first set of features that contain synthetic single stranded polynucleotides of no more than 100 nucleotides in length. (specification page 4, lines 13-20). Simply put, the claimed subject matter relates to polynucleotide arrays that contain two different types of features: single stranded cDNA features comprising complements of RNA molecules (e.g., comprising coding sequences and excluding intron sequences) which are at least 400 nucleotides in length and single stranded synthetic polynucleotide features which can comprise coding or non-coding sequences but are no more than 100 nucleotides in length.

The claimed subject matter provides a solution to problems associated with the use of polynucleotide arrays containing only a single type of feature, e.g., arrays containing only cDNA features *or* arrays containing only synthetic polynucleotide features. As described in the specification at page 3, line 21 through page 4, line 12, arrays comprising shorter length synthetic polynucleotides may lack sensitivity because they have been designed to the wrong region of a sample target (for example, a portion

not present within a specific splice variant or one containing a polymorphism that impacts hybridization). However, arrays comprising longer length cDNA probes may lack specificity and therefore be unable to detect expression differences within one member of a gene family if other members are present and unchanged or cross reactive with a different gene entirely. Further, the use of longer length probes necessitates the use of longer length control targets which are harder to manufacture, cost more and may be less stable.

In recognition of the problems associated with polynucleotide arrays containing a single type of feature, the claimed invention provides a polynucleotide array containing *two* types of features: cDNA features of at least 400 nucleotides and synthetic polynucleotide features of no more than 100 nucleotides, as discussed above. The two types of features provide complementary data that can be combined to provide higher quality and significantly more reliable, experimental results.

In the embodiments of the invention recited in claims 14 and 41, the sequences of the synthetic polynucleotides of the array are contained within the sequences of the cDNA molecules of the array (page 13, lines 26-28). In other words, the array recited in claims 14 and 41 contains a synthetic polynucleotide feature and a cDNA feature that should both hybridize to the same nucleic acid species in a sample exposed to the array since the sequence is one is contained within the sequence of the other (page 5 lines 10-13).

In the embodiments of the invention recited in claims 11-13, 15-20 and 39-40, less than 70% of the sequence of the synthetic polynucleotides is contained within the sequence of the cDNAs (page 12 lines 28-30) on the array. In these embodiments, features containing those polynucleotides may be employed to as controls, or to "fill in" for failed sequences (page 12 lines 30-31). Claims 15-20 are more specifically drawn to kits comprising such arrays further comprising control sequences which are at least about 70% complementary to a sequence of a second polynucleotide which is different for different ones of the controls.

GROUNDS OF REJECTION TO BE REVIEWED ON APPEAL

The grounds of rejection to be reviewed by the Board are:

I. ..... THE REJECTION OF CLAIMS 1 and 9 UNDER 35 U.S.C. §102(b) AS ANTICIPATED BY CLONTECH

II. ..... THE REJECTION OF CLAIMS 1-3, 5-10, 14, 38 and 41 UNDER 35 U.S.C. §103 AS OBVIOUS IN VIEW OF BAO AND BOBROW

III ..... THE REJECTION OF CLAIMS 11-13, 15-20 and 39-40 UNDER 35 U.S.C. §103 AS OBVIOUS IN VIEW OF BAO AND CLONTECHNIQUES

All of the appealed claims were finally rejected in the Final Office Action of August 17, 2004. Details of the above grounds of rejection may be found therein. Final Office Action of August 17, 2004 is termed "FOA" herein.

ARGUMENT

Each ground of rejection is argued separately below.

I. REJECTION OF CLAIMS 1 AND 9 UNDER 35 U.S.C. §102(c) BY CLONTECH

Claims 1 and 9 stand rejected under 35 U.S.C. § 102(b) as being anticipated by Clontech (the Clontech Catalog of 1995, page 26). The Examiner asserts that Fig. 4.2 shows an array of polynucleotides that anticipates the subject matter of claims 1 and 9.

The M.P.E.P. and current caselaw provide clear guidance on the requirements of an anticipatory reference:

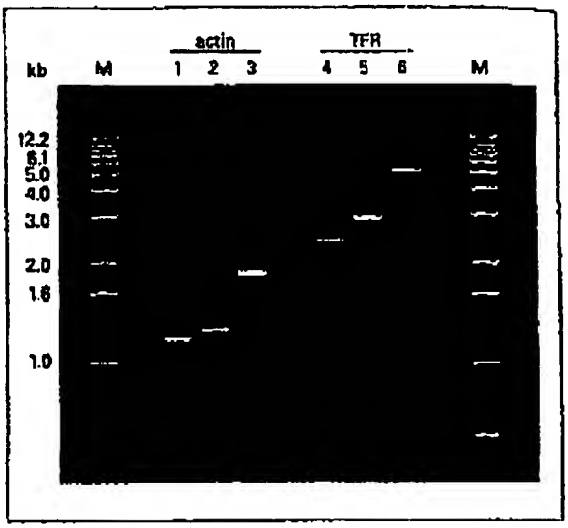
> A claim is anticipated only if each and every element as set forth in the claim is found, either expressly or inherently described, in a single prior art reference. The identical invention must be shown in as complete detail as it is contained in the ... claim. MPEP 3131 (citing Bros. v. Union Oil Co. of California, 814 F.2d 628, 631, 2 USPQ2d 1051, 1053 (Fed. Cir. 1987) and Brown v. 3M, 265 F.3d 1349, 1351, 60 USPQ2d 1375, 1376 (Fed. Cir. 2001)).

Claim 9 depends on claim 1. Claims 1 and 9 are therefore directed to a polynucleotide *array* containing ***single stranded*** cDNA molecules **of at least 400 nucleotides** and single stranded synthetic polynucleotides **of no more than 100 nucleotides** in length.

Accordingly, if Clonetech's Fig. 4.2 is to anticipate the claims, it should show,

among other things: a) a polynucleotide array, b) *single stranded* cDNA molecules **of at least 400 nucleotides** and c) synthetic polynucleotide of **no more than 100 nucleotides** in length.

For the convenience of the Board, Clonetech's Fig. 4.2 is reproduced below:



Clonetech's Fig. 4.2 shows a picture of an electrophoresis gel of PCR-amplified cDNA products that are all above 1 kb in length, according to the size markers on the left and right hand sides of the gel.

Clonetech's Fig. 4.2 therefore shows a picture of an electrophoresis gel, not a polynucleotide array. Accordingly, Clonetech's Fig. 4.2 fails to show a polynucleotide array, as required by the claims.

Further, Clonetech's Fig. 4.2 shows PCR-amplified cDNA products that are double-stranded, not single stranded. Accordingly, Clonetech's Fig. 4.2 fails to show single-stranded cDNA molecules, as required by the claims.

Finally, Clonetech's Fig. 4.2 does not show a synthetic polynucleotide of no more than 100 nucleotides in length, as required by the claims.

In view of the foregoing, the Appellants submit to the Board that Clonetech, as relied upon by the Examiner to establish this rejection, fails to disclose at least three features of the invention recited in claims 1 and 9.

Accordingly, Clontech falls well short of being an anticipatory publication.

In view of the foregoing discussion, the Appellants request that Board reverse this rejection.

II. REJECTION OF CLAIMS 1-3, 5-10, 14, 38 and 41 UNDER 35 U.S.C. §103 AS OBVIOUS IN VIEW OF BAO AND BOBROW

Claims 1-3, 5-10, 14, 38 and 41 stand rejected under 35 U.S.C. § 103(a) as being obvious over Bao (USPN 6,251,601) in view of Bobrow (USPN 6,399,299). The Examiner argues that Bao discloses a polynucleotide array containing different types of features that, in combination with Bobrow's polynucleotide array, renders the appealed claims obvious.

In establishing this rejection, the Examiner acknowledges that Bao is deficient because Bao does not specifically disclose an array containing cDNAs and oligonucleotides located at independent features (see FOA page 3, 3rd and 4th lines from the end: "While ***this passage does not specifically state members*** of the mixture ***are located at independent features....***"). (emphasis added). To meet Bao's deficiency, the Examiner cites Brobrow and simply states that "arrays comprising combinations of oligonucleotides and cDNAs were well known in at the time the claimed invention was made" (FOA page 4, lines 5-8).

The Appellants submit that this rejection is deficient because:

a) a polynucleotide array containing both cDNA elements and synthetic oligonucleotide elements of the recited size limitations is not suggested by either of the cited references; and

b) the proposed modification to Bao's polynucleotide array would render the Bao's polynucleotide array unsatisfactory for its intended purpose.

Further, and with particular respect to claims 14 and 41, neither Bao or Bobrow discloses any array containing synthetic polynucleotides having sequences that are contained within the sequences of cDNA molecules present on the array.

Support for the Appellants' position is set forth below.

In presenting the Appellants' position, arguments regarding claims 1-3, 5-10, 14, 38 and 41 will be presented first, followed by arguments particularly directed to claims 14 and 41.

a) Arguments regarding claims 1-3, 5-10, 14, 38 and 41

The M.P.E.P. provides clear guidance on the requirements of a *prima facie* case of obviousness:

> To establish a prima facie case of obviousness, three basic criteria must be met. First, there must be some suggestion or motivation, either in the references themselves or in the knowledge generally available to one of ordinary skill in the art, to modify the reference or to combine reference teachings. Second, there must be a reasonable expectation of success. Finally, the prior art reference (or references when combined) must teach or suggest all the claim limitations." M.P.E.P. § 2142.

Thus, the combined teachings of the cited references must teach or suggest all of the limitations of the claimed invention for the combined teaching to render the claimed invention obvious. Therefore, all of the elements of the claimed process must be taught or suggested by Bao and Bobrow in order for these references to render the claimed invention obvious.

Further, as noted in MPEP § 2143.01:

> "If proposed modification would render the prior art invention being modified unsatisfactory for its intended purpose, then there is no suggestion or motivation to make the proposed modification. In re Gordon, 733 F.2d 900, 221 USPQ 1125 (Fed. Cir. 1984)"

Accordingly, if a rejection proposes a modification to Bao's polynucleotide array that would render Bao's array unsuitable for its intended use, then the rejection should be withdrawn.

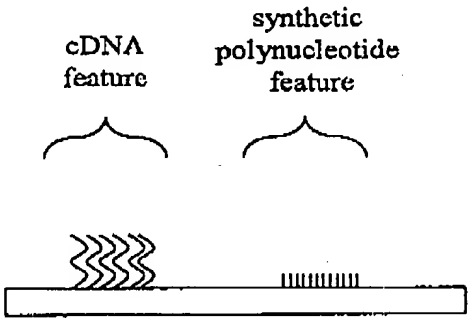
i. As cited, the combination of Bao and Bobrow does not suggest the claimed invention

Bao's disclosure is directed to methods and compositions for simultaneously analyzing gene expression and chromosomal abnormalities. (see Bao's title). Bao's arrays therefore contain probes for measuring genome abnormalities (e.g., long genomic DNA probes such as clones from a genomic library comprising one or more exons and one or more introns and ranging from 20,000 bp to about 250,000 bp; see col. 6, lines 56–60 and col. 8 lines 55-65), and probes for measuring mRNA expression. The probes for measuring mRNA expression can be synthetic oligomer probes or cDNA probes, both complementary to mRNA molecules or corresponding to coding sequences (see, e.g.,

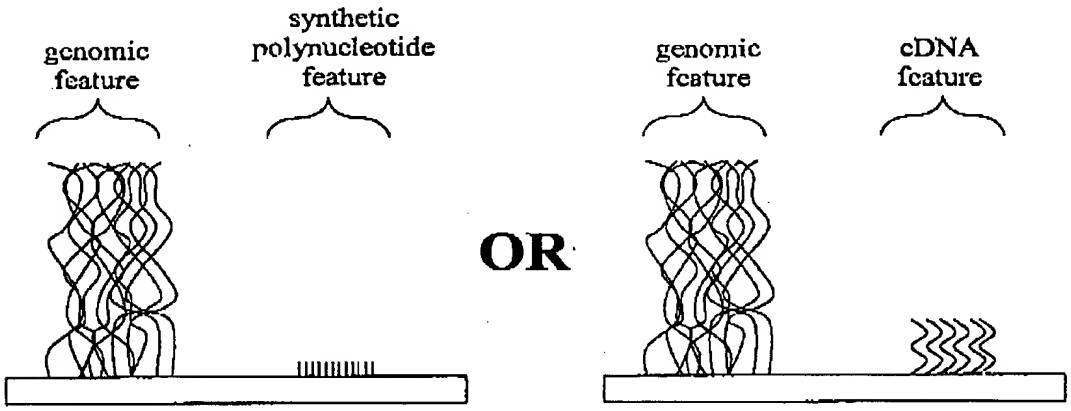
column 8, lines 39-44). Summarized in Bao's own words (see col. 3, lines 65-67), his methods involve "an array with a mixture of genomic DNA target elements and oligomer DNA **or** cDNA target elements, with the oligomer DNA/cDNA targets measuring expression and the genomic DNA targets measuring chromosomal change." (emphasis added).

Accordingly, Bao's arrays contain either genomic probes and cDNA probes, **or** genomic probes and oligonucleotide probes. Bao does not disclose any array containing independent cDNA probes of at least 400 nucleotides ***and*** polynucleotide probes of no more than 100 nucleotides, as required by the appealed claims.

In other words, the arrays recited in the Appealed claims contain cDNA features (i.e., comprising no intron sequences) of greater than 400 nucleotides ***and*** synthetic polynucleotide features of no more than 100 nucleotides, as illustrated by the following figure:



whereas Bao's arrays contain:



Case 1 Case 2

With respect to Case 1, Bao's synthetic polynucleotides (referred to in Bao as "oligomers") can range from 8 to 100 bp (col. 8, lines 27-31) and Bao's genomic feature sequences are greater than 400 bp (e.g., greater than 20kb). However, Bao's genomic features contain intron sequences and are thus distinguishable from the cDNA molecules of the claims. In other words, Bao's Case 1 array is distinguishable the claimed array because Bao's Case 1 array contains genomic features in combination with synthetic

polynucleotide features, not cDNA features in combination with synthetic polynucleotide features, as required by the appealed claims.

With respect to Case 2 and similar to the above, although greater than 400 bp, the genomic features of Bao do not qualify as cDNAs as claimed in the instant claims because they comprise intron sequences. Accordingly, Bao's Case 2 array is distinguishable the claimed array because Bao's Case 2 array contains genomic features in combination with cDNA features, not cDNA features in combination with synthetic polynucleotide features, as required by the appealed claims.

To the extent that Bao teaches that cDNAs can range from 100bp to 5000bp, nowhere does Bao teach or suggest providing an array containing cDNA sequences that are greater than 400 nucleotides in length ***and*** synthetic polynucleotides that are no longer than 100 nucleotides in length.

The fact that Bao does not specifically disclose an array containing independent cDNA probes ***and*** synthetic polynucleotide probes is acknowledged by the Examiner (See FOA page 3, lines 3rd and 4th lines from the bottom: Bao "does not specifically state members of the mixture are located at independent features"). Further, nowhere does Bao teach or suggest providing features comprising nucleic acid molecules which differ in size as recited in the claims.

Bao is therefore deficient in that it fails to disclose elements of the appealed claims. In order to meet Bao's deficiency and thereby attempt to establish a *prima facie* rejection, the Examiner has cited Bobrow. Bobrow is cited to show that "arrays comprising combinations of oligonucleotides and cDNAs were well known in at the time the claimed invention was made" (FOA page 4, lines 5-8). In order to support this statement, the Examiner points towards col. 3, lines 30-35 and claim 1 of Bobrow. However, a review of col. 3, lines 30-35 and claim 1 of Bobrow reveals that there is again no mention an array containing independent cDNA features ***and*** oligonucleotide features. In fact, the term "cDNA" is not even found in Bobrow's col. 3, lines 30-35. For the Board's convenience, Bobrow's col. 3, lines 30-35, is set forth below:

> "As discussed above, the members can comprise materials such as oligonucleotides, DNA and/RNA and/or fragments thereof, peptides, protein fragments, cell fragments, cells and tissues and each is capable of binding to

a specific material so as to form a specific binding pair."

Bobrow, like Bao, therefore fails to specifically describe an array containing oligonucleotide elements ***and*** cDNA elements that are independent of each other, and nowhere teaches or suggests providing nucleic acid probes at independent features which differ in size as recited in the claims.

Accordingly, Bao and Bobrow, taken independently or in any combination, fail to teach an element of the claims: an array containing independent oligonucleotide elements ***and*** cDNA elements with the recited size limitations stated in the claims.

In view of the foregoing discussion, the Appellants submit that the appealed claims cannot be rendered obvious by the combination of Bobrow and Bao because an element of the claims is not taught. In view of this, the Appellants submit to the Board that this rejection should be reversed.

ii. The proposed modification to Bao's polynucleotide array would render the Bao's polynucleotide array unsatisfactory for its intended purpose

As discussed above and pursuant to MPEP § 2143.01, if a rejection proposes a modification to Bao's polynucleotide array that would render Bao's array unsuitable for its intended use, then the rejection cannot be a *prima facie* rejection and should be withdrawn.

Bao's polynucleotide array is intended for use in simultaneous analysis of gene expression and chromosomal abnormalities.

The Appellants submit that if Bao's array was modified to be an array meeting the requirements of the rejected claims, e.g., to become an array of cDNAs and oligonucleotides, such an array would be unsatisfactory for Bao's intended use, i.e., unsatisfactory for detecting genomic abnormalities. This position is supported by the fact that Bao does not recognize the use of short genomic probes (less than 20kb) to examine chromosome abnormalities, therefore Bao provides no teaching or suggestion to provide arrays comprising features that include both cDNA and synthetic polynucleotide probes as required by the claims. In other words, if Bao's array was modified to become an array of cDNAs and oligonucleotides, it would not contain any genomic probes of the size taught by Bauer as necessary, and, as such, would become unsatisfactory for

examining chromosome abnormalities. Accordingly, the modification proposed by the Examiner would render Bao's array unsatisfactory for its intended purpose.

In view of the foregoing discussion and pursuant to MPEP § 2143.01, Bao's teachings, alone or in combination with any other reference, cannot render the rejected claims obvious. The Appellants submit to the Board that this rejection may also be reversed on this basis.

The Appellants note that this argument has been presented to the Examiner in the Appellants' response to the first and second Office Actions in this case. The Examiner has never addressed this argument.

b) Arguments regarding claims 14 and 41

Claims 14 and 41 recite an array in which the sequences of synthetic polynucleotides of an array are contained within sequences of the cDNA molecules of the array. In other words and as set forth with clarity in claim 41, the array contains (a) a first set of multiple features each of which comprises a cDNA molecule of at least 400 nucleotides in length; and (b) a second set of features independent of said first set of features each of which comprises a synthetic polynucleotide molecule comprising a nucleotide sequence that is also present in a single stranded cDNA of the first set of features and is of no more than 100 nucleotides in length.

The Appellants respectfully submit that neither Bao nor Bobrow teach such a feature, and, accordingly, this rejection should be reversed.

In the second Office Action, the Examiner cited Bao's Col. 8, lines 16-26 in support of the Office's position that Bao teaches oligonucleotides contained within cDNAs present on an array. However, the cited paragraph relates to polynucleotides *within* a single element (see "each target element can comprise a mixture of target nucleic acids of different lengths and sequences...." in Col. 8, lines 16-18), not polynucleotides present in *different* elements, as required by the instant claims. Neither Bao nor Bobrow suggests that certain elements may contain polynucleotides having a sequence that is contained within polynucleotides of other elements.

In the first paragraph of page 8 of the FOA, the Examiner appears to be attempting to indicate that there is no requirement in claim 14 or 41 that the sequence of a synthetic polynucleotide present on an array is also present in a sequence of a cDNA molecule present on the array. However, the Appellants submit that this is not the case.

For example, claim 41 clearly recites that the array "comprises a synthetic polynucleotide molecule *comprising a nucleotide sequence that is also present in a single stranded cDNA* of the first set of features". Accordingly, such a requirement is present in the claims, and has been ignored by the Examiner in establishing this rejection.

In view of the foregoing discussion, the Appellants submit that neither Bao or Bobrow discloses or even suggests a feature of claims 14 and 41. Accordingly this rejection is deficient and should be reversed.

III. THE REJECTION OF CLAIMS 11-13, 15-20 and 39-40 UNDER 35 U.S.C. §103 AS OBVIOUS IN VIEW OF BAO AND CLONTECHNIQUES

Claims 11-13, 15-20 and 39-40 are rejected under U.S.C. § 103(a) as being unpatentable over Bao (USPN 6,251,601) in view of CLONTECHniques (July 2000).

Claims 11-13, 15-20 and 39-40, like claims 1-3, 5-10, 14, 38 and 41, recite a polynucleotide array containing independent cDNA probes *and* oligonucleotide probes (as discussed above) in which at least 70% of the sequence of the oligonucleotide probes is not contained within the sequences of the cDNA molecules.

In order to establish this rejection, Bao is cited to provide a polynucleotide array containing independent cDNA probes and oligonucleotide probes, and CLONTECHniques is cited to provide control oligonucleotide probes (assertedly containing sequences that are not contained within cDNA probes), and kits.

For the same reasons as those set forth above, the Appellants submit that Bao is deficient for not specifically teaching a polynucleotide array containing independent cDNA probes *and* oligonucleotide probes. Also as discussed above, so much is acknowledged by the Examiner.

CLONTECHniques' control oligonucleotide probes do not meet the critical deficiency of Bao and, accordingly, Bao and CLONTECHniques, taken together or in any combination, fail to disclose an element of the invention recited in claims 11-13, 15-20 and 39-40.

Since this combination of references fails to disclose an element of claims 11-13, 15-20 and 39-40, this rejection is deficient and may be reversed.

In other words, Bao is deficient in that it fails to fairly suggest an array having a combination of cDNAs and synthetic oligonucleotides.

CLONTECHniques fails to meet Bao's deficiency, and, as such, the cited

references, taken separately or together, fail to fairly suggest the claimed subject matter: an array containing cDNAs of at least 400 nucleotides in length *and* synthetic polynucleotide molecules that are no more than 100 nucleotides in length.

Accordingly, the cited references cannot render the claimed subject matter obvious and this rejection may be reversed.

RELIEF REQUESTED

Appellants respectfully request that the rejection of claims 1-3, 5-20 and 38-41 under 35 U.S.C. §102(b) and 35 U.S.C. §103 be reversed, and that the application be remanded to the Examiner with instructions to issue a Notice of Allowance.

Respectfully submitted,
BOZICEVIC, FIELD & FRANCIS LLP

Date: Jan 11, 2005

By: _____
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APPENDIX OF PENDING CLAIMS

1. A polynucleotide array comprising:

(a) a first set of multiple features each of which comprises a single stranded cDNA molecule of at least 400 nucleotides in length; and

(b) a second set of features independent of said first set of features each of which comprises a synthetic single stranded second polynucleotide molecule of no more than 100 nucleotides in length.

2. A polynucleotide array according to claim 1 wherein a ratio of the first set of features to the second set of features is at least 10/1.

3. A polynucleotide array according to claim 1 wherein a ratio of the first set of features to the second set of features is at least 20/1.

4. **(Cancelled)**

5. A polynucleotide array according to claim 1 wherein the first cDNA molecules are from enzymatic processing of one or more longer polynucleotides.

6. A polynucleotide array according to claim 1 wherein the cDNA molecules have a length of at least 500 nucleotides.

7. A polynucleotide array according to claim 1 wherein the cDNA molecules have a length of at least 1000 nucleotides and the second polynucleotides have a length of no

more than 80 nucleotides.

8. A polynucleotide array according to claim 6 wherein the lengths of the first and second polynucleotides exclude the lengths of a polynucleotide stilt portion if present.

9. A polynucleotide array according to claim 1 wherein the array features are arranged in a rectangle with second set features at least at the corners of the rectangle.

10. A polynucleotide array according to claim 1 wherein the array features are arranged in lines, with at least some lines including features of both the first and second sets of features and in which lines at least two features of the second set of features are spaced apart by at least 70% of the first set features in the same line.

11. A polynucleotide array according to claim 1 wherein at least 70% of a sequence of a second polynucleotide molecule is not contained within a sequence of a cDNA molecule.

12. A polynucleotide array according to claim 11 wherein at least 70% of the sequences of more than half the second polynucleotide molecules is not contained within a sequence of a cDNA molecule.

13. A polynucleotide array according to claim 1 wherein none of the sequences of the second polynucleotide molecules is contained within a sequence of a cDNA molecule.

14. A polynucleotide array according to claim 1 wherein the sequence of a second

polynucleotide is contained within a cDNA molecule sequence.

15. A kit comprising:

(a) a polynucleotide array having:

a first set of multiple features each of which comprises a single stranded cDNA molecule of at least 400 nucleotides in length;

a second set of features each of which comprises a synthetic single stranded second polynucleotide molecule of no more than 100 nucleotides in length; and

(b) polynucleotide controls each of which is, or their complement is, at least 70% complementary to a sequence of a second polynucleotide which is different for different ones of the controls.

16 A kit according to claim 15 wherein each of the controls or their compliments is at least 90% complementary to a sequence of a second polynucleotide which is different for different ones of the controls.

17. A kit according to claim 15 wherein the controls are labeled.

18. A kit according to claim 15 wherein a ratio of the first set of features to the second set of features is at least 10/1.

19. A kit according to claim 15 wherein a ratio of the first set features to the second set of features is at least 20/1.

20. A kit according to claim 15 additionally comprising instructions to expose the

array to a sample and the controls or their complements.

21-37. **(Cancelled)**

38. A polynucleotide array according to claim 1 wherein features of the second set of features have the same polynucleotide.

39. A polynucleotide array according to claim 1 wherein at least 70% of a sequence of each of the second polynucleotide molecules is not contained within a sequence of a cDNA molecule.

40. A polynucleotide array according to claim 1 wherein at least 70% of a sequence of each of the second polynucleotide molecules is not contained within a sequence of any of the cDNA molecules.

41. A polynucleotide array comprising:

(a) a first set of multiple features each of which comprises a cDNA molecule of at least 400 nucleotides in length; and

(b) a second set of features independent of said first set of features each of which comprises a synthetic polynucleotide molecule comprising a nucleotide sequence that is also present in a single stranded cDNA of the first set of features and is of no more than 100 nucleotides in length.